510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
DEVICE ONLY TEMPLATE

A. 510(k) Number:

k041657

B. Purpose for Submission:

New Device

C. Analyte:

Angiotensin Converting Enzyme (ACE)

D. Type of Test:

Quantitative Immunoassay

E. Applicant:

Thermo Electron Corporation

F. Proprietary and Established Names:

Thermo Electron Corporation Infinity™ ACE Liquid Stable Reagent (Angiotensin Converting Enzyme)

G. Regulatory Information:

1. Regulation section:
   21 CFR § 862.1090 (Angiotensin converting enzyme (A.C.E.) test system.)
   21 CFR § 862.1150 (Calibrator)
   21 CFR § 862.1660 (Quality control material (assayed and unassayed)

2. Classification:
   Class II
   Class II
   Class I

3. Product Code:
   KQN
   JIS
   JJX

4. Panel:
   Clinical Chemistry

H. Intended Use:

1. Intended use / Indications for Use:

   The Thermo Electron Infinity™ ACE Reagent Kit is intended for the quantitative determination of ACE in human serum or plasma. The product is for in vitro diagnostic use only.

   Measurements obtained by this device are used in the diagnosis and treatment of diseases such as sarcoidosis, a disease characterized by the formation of nodules in the lungs, bones, and skin, and Gaucher`s disease, a hereditary disorder affecting the spleen.

   The Thermo Electron Infinity™ ACE Calibrator is intended for the calibration of ACE assays. The product is for in vitro diagnostic use only.

   The Thermo Electron Infinity™ ACE Normal and Elevated Controls are intended for monitoring the accuracy and precision of ACE assays. The product is for in vitro diagnostic use only.

2. Special condition for use statement(s):
   Prescription Use Only

3. Special instrument Requirements:
   This reagent can be adapted for both manual and automated applications. Requirements include a temperature of 37^{o} C and the ability to read the absorbance at 340 nm.

I. Device Description:

The reagent comes in a ready to use liquid form. The active ingredients are N-[3-(2-furyl)-acryloyl]-L-phenyl-alanylglyclglycine (FAPGG) at greater than 0.40 mmol/L and Tris buffer at 55 mmol/L. The reagent also contains non-reactive fillers and stabilizers.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Sigma Diagnostics Angiotensin Converting Enzyme (ACE) Reagent

2. Predicate k number(s):
   k854245

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Indications for Use	Same	Quantitative Determination of ACE in serum or plasma
Methodology	Same	Immunoassay: FAPGG hydrolyzed to FAP (furylacryloylphenylalanine) and glycylglycone
Upper Reportable Concentration	Same	120 U/L
Differences		
Item	**Device**	**Predicate**
Reagent Form	Liquid Ready to Use	Lyophilized

K. Standard/Guidance Document Referenced (if applicable):

The sponsor referenced NCCLS EP5: Evaluation of Precision Performance of Clinical Chemistry Devices

L. Test Principle:

The assay reaction is based on the method of Holmquist et al. In this method the direct substrate N-[3-(2-furyl)-acryloyl]-L-phenyl-alanylglyclglycine is hydrolyzed to N-[3-(2-furyl)-acryloyl]-L-phenyl-alanine and glycylglycine:

$$\text{FAPGG} \xrightarrow{\text{ACE}} \text{FAP + glycylglycine}$$

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The sponsor presented the following precision data for the Cobas Mira using NCCLS EP-5 protocol:

		Level I	Level II
Within run precision	N	80	80
	Mean (U/L)	35	90
	SD (U/L)	2.4	2.0
	CV (%)	6.9	2.3
Total precision	N	80	80
	Mean (U/L)	35	90
	SD (U/L)	3.7	5.1
	CV (%)	10.8	5.7

b. Linearity/assay reportable range:

Linearity was assessed by preparing a stock solution with an ACE concentration of at least 10% greater than the claimed upper reportable concentration. Dilutions of the stock solution from 0 to 100% are made with saline and analyzed as unknowns and plotted vs. the target concentration. This plot is examined visually for a linear relationship. In addition, the straight line of best fit is drawn through the data points and compared against a polynomial regression curve of best fit. The deviation of the polynomial regression line from the straight line of best fit must be less than 5%. The upper limit of linearity is defined as the concentration at which the polynomial regression curve deviates from the straight line of best fit by 5%. The reportable range was determined to be 1 to 120 U/L.

c. Traceability, Stability, Expected values (controls, calibrators, or method):

Calibrators and controls were previously cleared under K930477 and K860453, respectively, and preparation, storage, stability and traceability were addressed in those submissions. In the current submission, the sponsor is relabeling the previously cleared calibrators and controls and reassigning ACE values using the Thermo ACE reagent.

d. Detection limit:

The analytical sensitivity of 1.0 U/L was calculated by multiple measurements of a zero concentration sample. The mean and standard deviation of the dataset were calculated, and the analytical sensitivity was defined as the mean concentration plus two standard deviations.

e. Analytical specificity:

The sponsor evaluated the effects of hemoglobin, conjugated and unconjugated bilirubin, and triglycerides (Intralipid). No interference was defined as less than +/- 10% deviation from a neat sample. The following compounds showed no interference up to the concentration listed:

Hemoglobin: 725 mg/dL
Unconjugated Bilirubin: 13 mg/dL
Conjugated Bilirubin: 20 mg/dL
Triglycerides: 1000 mg/dL

EDTA was shown to inhibit ACE. Users are informed in the Package Insert that EDTA plasma is not an acceptable specimen.

f. Assay cut-off:
N/A

2. Comparison studies:
   a. Method comparison with predicate device:
   The sponsor compared 108 serum samples using the predicate device and the Thermo ACE reagent. Concentrations ranged from 1 to 114 U/L as measured by the Thermo ACE reagent. Linear regression analysis produced the following data:

   Thermo ACE = 0.961 Predicate – 3.3

   Correlation Coefficient (r) = 0.98

   b. Matrix comparison:
   This assay can measure ACE in either serum or heparinized plasma. The sponsor demonstrated equivalence between the two matrices by assaying six paired serum and heparinized samples, ranging in concentration from approximately 20 to 120 U/L. The heparinized samples had a mean % recovery of serum values of 96%.

3. Clinical studies:
   a. Clinical sensitivity:
   NA
   b. Clinical specificity:
   NA
   c. Other clinical supportive data (when a and b are not applicable):

4. Clinical cut-off:
   N/A
5. Expected values/Reference range:
   8 – 52 U/L (at 37^{o} C)

N. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.